

ILE 'HOME' ENTERED AT 22:36:37 ON 22 AUG 2008

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FILE 'CAPLUS' ENTERED AT 22:36:58 ON 22 AUG 2008
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FILE 'BIOSIS' ENTERED AT 22:36:58 ON 22 AUG 2008
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=> "positive charged (s) antigen"
L1 0 "POSITIVE CHARGED (S) ANTIGEN"

=> positive (w) charged
L2 21095 POSITIVE (W) CHARGED

=> antigen
L3 902001 ANTIGEN

=> L2 (l) L3
L4 281 L2 (L) L3

=> L2 (p) L3
L5 281 L2 (P) L3

=> L2 (s) L3
L6 73 L2 (S) L3

=> HCV
L7 42824 HCV

=>
=> L7 (s) L6
L8 1 L7 (S) L6

=> L7 (L) L6
L9 1 L7 (L) L6

=> L6 and L7
L10 1 L6 AND L7

=> adjuvant
L11 110859 ADJUVANT

=> L11 and L6
L12 16 L11 AND L6

=> D L8 IBIB ABS

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:396697 CAPLUS
DOCUMENT NUMBER: 135:4467
TITLE: Vaccine compositions
INVENTOR(S): Drane, Debbie; Cox, John; Houghton, Michael; Paliard, Xavier
PATENT ASSIGNEE(S): Csl Limited, Australia; Chiron Corporation

SOURCE: PCT Int. Appl., 67 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001037869	A1	20010531	WO 2000-AU1410	20001117
WO 2001037869	A9	20020718		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2391843	A1	20010531	CA 2000-2391843	20001117
AU 2001013730	A	20010604	AU 2001-13730	20001117
AU 772617	B2	20040506		
EP 1239876	A1	20020918	EP 2000-975681	20001117
EP 1239876	B1	20080730		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 518999	A	20021220	NZ 2000-518999	20001117
JP 2003514872	T	20030422	JP 2001-539483	20001117
NZ 520976	A	20050128	NZ 2000-520976	20001117
ZA 2002003986	A	20031217	ZA 2002-3986	20020520
US 20040191270	A1	20040930	US 2003-622470	20030721
			US 1999-166652P	P 19991119
			US 2000-224362P	P 20000811
			US 2000-714438	B1 20001117
			WO 2000-AU1410	W 20001117

PRIORITY APPLN. INFO.:

AB The present invention relates generally to an immunogenic complex comprising a charged organic carrier and a charged antigen and, more particularly, a neg. charged organic carrier and a pos. charged antigen, wherein the charged antigen is a polyprotein of Hepatitis C Virus (HCV), particularly the core protein of HCV, or a fragment thereof, or a fusion protein comprising the polyprotein or a fragment thereof. The complexes of the present invention are useful in vaccine compns. as therapeutic and/or prophylactic agents for facilitating the induction of immune responses, and in particular a cytotoxic T-lymphocyte response, in the treatment of a disease condition which results from an HCV infection.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> D L12 IBIB ABS 1-16

L12 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2004:975071 CAPLUS
 DOCUMENT NUMBER: 142:416911
 TITLE: Structure and adsorption properties of commercial calcium phosphate adjuvant
 AUTHOR(S): Jiang, Dongping; Premachandra, Gnanasiri S.; Johnston, Cliff; Hem, Stanley L.
 CORPORATE SOURCE: Department of Industrial and Physical Pharmacy, Purdue

SOURCE: University, West Lafayette, IN, 47907-2091, USA
Vaccine (2004), 23(5), 693-698
CODEN: VACCDE; ISSN: 0264-410X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Calcium phosphate adjuvant is a com. available vaccine adjuvant that potentiates the immune response to antigens. Although its name suggests that it is $\text{Ca}_3(\text{PO}_4)_2$, x-ray diffraction, FTIR spectroscopy, thermal anal. and the Ca/P molar ratio identify com. calcium phosphate adjuvant as non-stoichiometric hydroxyapatite, $\text{Ca}_{10-x}(\text{HPO}_4)_x(\text{PO}_4)_{6-x}(\text{OH})_{2-x}$, where x varies from 0 to 2. The surface charge is pH-dependent (point of zero charge = 5.5). Consequently, com. calcium phosphate adjuvant exhibits a neg. surface charge at physiol. pH and electrostatically adsorbs pos. charged antigens. The presence of hydroxyls allows calcium phosphate adjuvant to adsorb phosphorylated antigens by ligand exchange with surface hydroxyls.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:350514 CAPLUS
DOCUMENT NUMBER: 138:95296

TITLE: Adjuvant effect of zinc on microencapsulated tetanus toxoid

AUTHOR(S): McHugh, C.; Somavarapu, S.; Atuah, K.; Eyles, J.; Alpar, O.

CORPORATE SOURCE: Centre for Drug Delivery Research, University of London School of Pharmacy, Bloomsbury, London, WC1N 1AX, UK

SOURCE: Proceedings - 28th International Symposium on Controlled Release of Bioactive Materials and 4th Consumer & Diversified Products Conference, San Diego, CA, United States, June 23-27, 2001 (2001), Volume 2, 1083-1084. Controlled Release Society: Minneapolis, Minn.

CODEN: 69CNY8

DOCUMENT TYPE: Conference

LANGUAGE: English

AB The object of this study was to investigate the adjuvant effect of zinc (as zinc oxide) on the adjuvanticity of microencapsulated tetanus toxoid. We also investigated the effect of surface modification of the zinc oxide particles in order to increase the immune response obtained using zinc alone as an adjuvant. The microencapsulation of zinc oxide with the antigen was found to increase the immune response generated and coating the zinc oxide particles in order to make them more pos. charged was found to increase the immune titer compared with uncoated particles.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:314786 CAPLUS
DOCUMENT NUMBER: 136:324057

TITLE: Vaccine composition comprising an adjuvant /carrier peptide which enhances immune response to a co-administered antigen

INVENTOR(S): Fritz, Joerg; Mattner, Frank; Zauner, Wolfgang; Nagy, Eszter; Buschle, Michael

PATENT ASSIGNEE(S): Cistem Biotechnologies G.m.b.H., Austria

SOURCE: PCT Int. Appl., 40 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032451	A1	20020425	WO 2001-EP12041	20011018
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AT 2000001789	A	20021115	AT 2000-1789	20001018
AT 410635	B	20030625		
CA 2426490	A1	20020425	CA 2001-2426490	20011018
AU 2002012326	A	20020429	AU 2002-12326	20011018
AU 2002212326	B2	20060105		
EP 1326634	A1	20030716	EP 2001-980496	20011018
EP 1326634	B1	20060426		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 2003002117	A2	20030929	HU 2003-2117	20011018
HU 2003002117	A3	20041129		
BR 2001014994	A	20030930	BR 2001-14994	20011018
JP 2004511528	T	20040415	JP 2002-535688	20011018
NZ 524532	A	20041029	NZ 2001-524532	20011018
AT 324116	T	20060515	AT 2001-980496	20011018
PT 1326634	T	20060929	PT 2001-980496	20011018
ES 2263668	T3	20061216	ES 2001-980496	20011018
RU 2328305	C2	20080710	RU 2003-114434	20011018
ZA 2003001465	A	20040224	ZA 2003-1465	20030224
IN 2003MN00263	A	20050304	IN 2003-MN263	20030226
MX 2003PA02828	A	20030714	MX 2003-PA2828	20030331
NO 2003001595	A	20030605	NO 2003-1595	20030408
US 20050063978	A1	20050324	US 2003-399442	20030417
HK 1055899	A1	20061201	HK 2003-108189	20031112
PRIORITY APPLN. INFO.:				
		AT 2000-1789	A	20001018
		EP 2001-980496	A	20011018
		WO 2001-EP12041	W	20011018

AB The invention relates to a vaccine which comprises at least one antigen and a peptide comprising a sequence R1-XZXNXZX-R2, whereby N is a whole number between 3 and 7, preferably 5, -X is a pos. charged natural and/or non-natural amino acid residue, Z is an amino acid residue selected from the group consisting of L, V, I, F and/or W, and R1 and R2 are selected independently from the other from the group consisting of -H, -NH₂, -COCH₃, -COH, a peptide with up to 20 amino acid residues or a peptide reactive group or a peptide linker with or without a peptide; X-R2 may also be an amide, ester or thioester of the C-terminal amino acid residue, as well as the use of said peptide for the preparation of an adjuvant for enhancing the immune response to at least one antigen. One example discusses the efficiency of peptide KLKLLLLKLK in delivery of influenza hemagglutinin antigen to antigen-presenting cells and uptake into APCs. The peptide also enhances T-cell responses (i.e. interferon- γ production) to the

antigen.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:396697 CAPLUS
DOCUMENT NUMBER: 135:4467
TITLE: Vaccine compositions
INVENTOR(S): Drane, Debbie; Cox, John; Houghton, Michael; Paliard, Xavier
PATENT ASSIGNEE(S): CSL Limited, Australia; Chiron Corporation
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001037869	A1	20010531	WO 2000-AU1410	20001117
WO 2001037869	A9	20020718		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2391843	A1	20010531	CA 2000-2391843	20001117
AU 2001013730	A	20010604	AU 2001-13730	20001117
AU 772617	B2	20040506		
EP 1239876	A1	20020918	EP 2000-975681	20001117
EP 1239876	B1	20080730		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 518999	A	20021220	NZ 2000-518999	20001117
JP 2003514872	T	20030422	JP 2001-539483	20001117
NZ 520976	A	20050128	NZ 2000-520976	20001117
ZA 2002003986	A	20031217	ZA 2002-3986	20020520
US 20040191270	A1	20040930	US 2003-622470	20030721
PRIORITY APPLN. INFO.:				
		US 1999-166652P	P	19991119
		US 2000-224362P	P	20000811
		US 2000-714438	B1	20001117
		WO 2000-AU1410	W	20001117

AB The present invention relates generally to an immunogenic complex comprising a charged organic carrier and a charged antigen and, more particularly, a neg. charged organic carrier and a pos. charged antigen, wherein the charged antigen is a polyprotein of Hepatitis C Virus (HCV), particularly the core protein of HCV, or a fragment thereof, or a fusion protein comprising the polyprotein or a fragment thereof. The complexes of the present invention are useful in vaccine compns. as therapeutic and/or prophylactic agents for facilitating the induction of immune responses, and in particular a cytotoxic T-lymphocyte response, in the treatment of a disease condition which results from an HCV infection.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2000:786836 CAPLUS
 DOCUMENT NUMBER: 134:339301
 TITLE: Evaluation of a liposome-supplemented intranasal influenza subunit vaccine in a murine model system: Induction of systemic and local mucosal immunity
 AUTHOR(S): de Haan, Aalzen; van Scharrenburg, Guus J. M.; Masihi, K. Noel; Wilschut, Jan
 CORPORATE SOURCE: Department of Medical Microbiology, Molecular Virology Section, University of Groningen, Groningen, 9713 AV, Neth.
 SOURCE: Journal of Liposome Research (2000), 10(2 & 3), 159-177
 CODEN: JLREE7; ISSN: 0898-2104
 PUBLISHER: Marcel Dekker, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The study reports on the mucosal immunoadjuvant activity of liposomes in an exptl. influenza subunit vaccine administered intranasally (i.n.) to mice. Antibody responses induced by the i.n. liposomal vaccine were compared to those induced by an influenza infection or by s.c. injection of subunit antigen alone, the conventional route of human flu vaccination. Neg. charged liposomes, but not pos. charged or zwitterionic liposomes, co-administered i.n. with influenza subunit antigen, stimulated systemic IgG levels and local antibody responses in pulmonary secretions, relative to the responses upon i.n. administration of subunit antigen alone. I.n. immunization with liposome-supplemented subunit antigen as well as s.c. immunization with subunit antigen alone or infection induced high levels of IgG antibodies in serum and pulmonary secretions, with a preferential induction of IgG1 upon immunization and IgG2a upon infection. Both i.n. immunization with liposome-supplemented antigen and infection, but not s.c. immunization with subunit antigen alone, induced local secretion of S-IgA. At the same time, both IgA- and IgG-secreting cells appeared in the lungs and lung-associated lymph nodes, suggestive of local antibody production. Thus, the liposomal adjuvant system, combined with a mucosal administration protocol, provides a promising strategy for induction of both systemic and local antibody responses against influenza virus.
 REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2000:592580 CAPLUS
 DOCUMENT NUMBER: 133:191986
 TITLE: Immunogenic complexes and methods relating thereto
 INVENTOR(S): Cox, John Cooper; Drane, Debbie Pauline
 PATENT ASSIGNEE(S): CSL Limited, Australia
 SOURCE: PCT Int. Appl., 111 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000048630	A1	20000824	WO 2000-AU110	20000217
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,				

SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 CA 2362204 A1 20000824 CA 2000-2362204 20000217
 AU 2000026515 A 20000904 AU 2000-26515 20000217
 AU 783344 B2 20051020
 EP 1150710 A1 20011107 EP 2000-904734 20000217
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO
 JP 2002537271 T 20021105 JP 2000-599420 20000217
 NZ 513935 A 20040227 NZ 2000-513935 20000217
 ZA 2001006521 A 20030310 ZA 2001-6521 20010808
 PRIORITY APPLN. INFO.: AU 1999-8735 A 19990217
 AU 1999-1861 A 19990727
 WO 2000-AU110 W 20000217

AB The present invention relates generally to an immunogenic complex comprising a charged organic carrier and a charged antigen and, more particularly, a neg. charged organic carrier and a pos. charged antigen. The complexes of the present invention are useful, *inter alia*, as therapeutic and/or prophylactic agents for facilitating the induction of a cytotoxic T-lymphocyte response to an antigen.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2000:526177 CAPLUS
 DOCUMENT NUMBER: 134:250883
 TITLE: Influence of antigenic forms and adjuvants on protection against a lethal infection of Aujeszky's disease virus
 AUTHOR(S): Katayama, S.; Oda, K.; Ohgitani, T.
 CORPORATE SOURCE: Division of Veterinary Microbiology, Kyoto Biken Laboratories, Uji, Kyoto, 611-0041, Japan
 SOURCE: Vaccine (2000), 19(1), 54-58
 CODEN: VACCDE; ISSN: 0264-410X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The influence of antigenic forms and adjuvant types on protection against a lethal infection of Aujeszky's disease virus (ADV) in mice was investigated. Antiviral IgG2a antibody response against particulate (inactivated ADV) and soluble antigen (ADV solubilized with deoxycholate-Na) in approx. order of extent was ISA70 > QS-21 > pos. charged liposome > neg. charged liposome > weak neg. charged liposome > ISA25 > lablabside F saponin > aluminum phosphate gel > non adjuvant. Particulate antigen induced higher IgG2a antibody production than soluble antigen. Particulate antigen combined with ISA70, ISA25 or pos. charged liposome gave 100, 50 and 40% protection to mice, resp. In contrast, soluble antigen plus ISA70 conferred 30% protection on mice. Immunogens using the other adjuvants gave \leq 20% protection to mice. These results indicate that a combination of particulate antigen and an appropriate adjuvant effectively induces the production of antiviral IgG2a antibody and provides protection against a lethal ADV infection in mice.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 1999:557808 CAPLUS

DOCUMENT NUMBER: 131:341812
TITLE: Positively charged liposome functions as an efficient immunoadjuvant in inducing cell-mediated immune response to soluble proteins
AUTHOR(S): Nakanishi, T.; Kunisawa, J.; Hayashi, A.; Tsutsumi, Y.; Kubo, K.; Nakagawa, S.; Nakanishi, M.; Tanaka, K.; Mayumi, T.
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Osaka University, Osaka, Japan
SOURCE: Journal of Controlled Release (1999), 61(1-2), 233-240
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In order to design an optimized liposome immunoadjuvant for inducing cell-mediated immune response against soluble proteinaceous antigens, we investigated the effect of liposomal surface charge on the immunoadjuvant action. Pos. charged liposomes containing soluble antigens functioned as a more potent inducer of antigen-specific cytotoxic T lymphocyte responses and delayed type hypersensitivity response than neg. charged and neutral liposomes containing the same concns. of antigens. To clarify the reason of the differential immune response, we examined the delivery of soluble proteins by the liposomes into the cytoplasm of macrophages, using fragment A of diphtheria toxin (DTA) as a marker. We found that pos. charged liposomes encapsulating DTA are cytotoxic to macrophages, while empty pos. charged liposomes, DTA in neg. charged and neutral liposomes are not. Consistent with this, only macrophages pulsed with OVA in pos. charged liposomes could significantly stimulate OVA-specific, class I MHC-restricted T cell hybridoma. These results suggest that the pos. charged liposomes can deliver proteinaceous antigens efficiently into the cytoplasm of the macrophages/antigen-presenting cells, where the antigens are processed to be presented by class I MHC mols. to induce the cell-mediated immune response. Possible development of a safe and effective vaccine is discussed.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:497103 CAPLUS
DOCUMENT NUMBER: 129:274369
ORIGINAL REFERENCE NO.: 129:55933a, 55936a
TITLE: Cationization of liposomal surface charge enhances adjuvant effect of liposomes for tumor vaccine
AUTHOR(S): Nakanishi, Tsuyoshi; Kunisawa, Jun; Hayashi, Akira; Tsutsumi, Yasuo; Hayakawa, Takao; Mayumi, Tadanori
CORPORATE SOURCE: Graduate School of Pharmaceutical Science, Osaka University, Suita, Osaka, 565-0871, Japan
SOURCE: Yakuzaigaku (1998), 58(2), 59-68
CODEN: YAKUA2; ISSN: 0372-7629
PUBLISHER: Nippon Yakuzaigaku Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In order to design an optimum liposome immunoadjuvant for tumor vaccines, we investigated the relationship between liposome surface charge and adjuvant action. Pos. charged multilamellar vesicles (MLVs) were taken up efficiently by macrophages, while neg. charged and neutral MLVs were hardly picked up. Consistent with this, pos. charged MLVs containing soluble ovalbumin (OVA) functioned as a more potent inducer of antigen-specific cytotoxic T lymphocyte (CTL) responses and antibody production than neg. charged and neutral MLVs containing

the same concns. of antigens. Furthermore, the in vivo anti-tumor effects of variously charged liposomal antigens were examined using a Meth A tumor model and a crude butanol extract derived from Meth A (Meth A-CBE) as the tumor-associated antigen. Mice vaccinated with pos. charged MLVs containing Meth A-CBE showed significant inhibition of Meth A tumor growth compared to mice vaccinated with Meth A-CBE alone or mice vaccinated with neutral or neg. charged liposomal Meth A-CBE. The injection of carrageenan into mice led to a significant loss of anti-tumor vaccinal effect of pos. charged liposomal Meth A-CBE, which may be due to the inhibition of uptake and antigen presentation of liposomal antigens by macrophages as a result of a lack of macrophages in the immune site. Our results indicate that the pos. charge on the surface of liposomes represents an important factor for enhancing their immunoadjuvancy in the induction of antigen-specific immune responses and vaccinal effects against tumors.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:775527 CAPLUS

DOCUMENT NUMBER: 128:66384

ORIGINAL REFERENCE NO.: 128:12895a,12898a

TITLE: Positively charged liposome functions as an efficient immunoadjuvant in inducing immune responses to soluble proteins

AUTHOR(S): Nakanishi, Tsuyoshi; Kunisawa, Jun; Hayashi, Akira; Tsutsumi, Yasuo; Kubo, Kazuyoshi; Nakagawa, Shinkasu; Fujiwara, Hiromi; Hamaoka, Toshiyuki; Mayumi, Tadanori

CORPORATE SOURCE: Faculty and Graduate School of Pharmaceutical Science, Osaka University, Suita, 565, Japan

SOURCE: Biochemical and Biophysical Research Communications (1997), 240(3), 793-797

CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To design an optimum liposome immunoadjuvant for soluble protein antigens, the authors investigated the relationship between liposomal surface charge and adjuvant action. Pos. charged multilamellar vesicles (MLV) were taken up efficiently by macrophages, while neg. charged and neutral MLVs were hardly picked up. Consistent with this, pos. charged MLVs containing soluble chicken egg albumin (OVA) functioned as a more potent inducer of antigen-specific cytotoxic T lymphocyte (CTL) responses and antibody production than neg. charged and neutral MLVs containing the same concns. of antigens. The pos. charge on the surface of liposomes represents an important factor for enhancing their immunoadjuvancy in the induction of antigen-specific immune responses.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:351527 CAPLUS

DOCUMENT NUMBER: 127:85895

ORIGINAL REFERENCE NO.: 127:16405a,16408a

TITLE: Adjuvanticity and protective immunity elicited by Leishmania donovani antigens encapsulated in positively charged liposomes

AUTHOR(S): Afrin, Farhat; Ali, Nahid

CORPORATE SOURCE: Leishmania Group, Indian Institute Chemical Biology, Calcutta, 700032, India

SOURCE: Infection and Immunity (1997), 65(6), 2371-2377

CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the search for a leishmaniasis vaccine, extensive studies of cutaneous leishmaniasis have been carried out. Investigations in this regard with the visceral form are limited. As an initial step in the identification of the protective mols., leishmanial antigens extracted from the membranes of *Leishmania donovani* promastigotes, alone or in association with liposomes, were evaluated for their immunogenicity and ability to elicit a protective immune response against challenge infection. I.p. immunization of hamsters and BALB/c mice with the leishmanial antigens conferred protection against infection with the virulent promastigotes. Encapsulation in pos. charged liposomes significantly enhanced the protective efficacy of these antigens. The splenic parasite burden of hamsters was reduced by 97% after 6 mo of infection. BALB/c mice exhibited 87 and 81.3% protection in the liver and spleen, resp., after 4 mo of infection. These protected animals elicited profound delayed-type hypersensitivity and increased levels of Leishmania-specific IgG antibodies. Protection in mice also coincided with elevated levels of IgM and IgA antibodies, which decreased with disease progression in the control-infected animals. Although both IgG1 and IgG2a antibodies were present in the sera of infected mice, IgG1 appeared to be the predominant isotype, suggesting a preferential induction of the Th2 type of immune response over that of Th1. Effective stimulation of all the IgG isotypes, particularly IgG2a, after immunization with liposome encapsulated antigens seems to be responsible for the significant of resistance against the disease. Taken together, these data indicate a potential for the liposomal antigens as a vaccine which could trigger both humoral and cell-mediated immune responses.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:254536 CAPLUS
DOCUMENT NUMBER: 122:38664
ORIGINAL REFERENCE NO.: 122:7363a, 7366a
TITLE: Interactions in model vaccines composed of mixtures of aluminum-containing adjuvants
AUTHOR(S): Al-Shakhshir, Ragheb H.; Lee, Ann L.; White, Joe L.; Hem, Stanley L.
CORPORATE SOURCE: Dep. Industrial and Physical Pharmacy, Purdue Univ., West Lafayette, IN, 47907, USA
SOURCE: Journal of Colloid and Interface Science (1995), 169(1), 197-203
CODEN: JCISA5; ISSN: 0021-9797
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The optimum formulation of vaccines containing multivalent antigens may require that more than a single type of aluminum-containing adjuvant be used. In some cases, in order to maximize the binding of the neg. charged antigen(s), a pos. charged adjuvant such as aluminum hydroxide could be used. In other cases, if the antigen(s) were pos. charged, a neg. charged adjuvant such as aluminum phosphate might be preferred. The multivalent vaccine would therefore be prepared by combining the individual monovalent bulks resulting in a suspension consisting of mixed aluminum-containing adjuvants. Studies of such mixed suspensions revealed that some phosphate ions from the aluminum phosphate adjuvant desorbed upon the dilution which occurred when the

monovalent bulks were combined. The desorption of phosphate reduced the neg. surface charge of the aluminum phosphate adjuvant. The desorbed phosphate anions were subsequently readsorbed by the aluminum hydroxide adjuvant resulting in a decrease of its pos. surface charge. Desorption of the adsorbed antigens may also occur when the monovalent suspensions are mixed. In the model system studied, a significant fraction (25%) of adsorbed lysozyme desorbed from the aluminum phosphate adjuvant upon dilution (1:2). In contrast, almost no bovine serum albumin was desorbed from an aluminum hydroxide adjuvant upon similar dilution. A method based on measuring the electrophoretic mobility of the adjuvants was developed to assess the interactions that take place between the different adjuvants. Rapid aggregation was observed for the system consisting of oppositely charged adjuvants. The rate of aggregation of the pos. charged aluminum hydroxide adjuvant with the neg. charged aluminum phosphate adjuvant was reduced by the adsorption of proteins. Colloidal stability was enhanced by increased surface coverage of the proteins on the adjuvants. It was concluded that protein adsorption reduces the rate of aggregation of the mixed adjuvant system by minimizing the difference in surface charge between the aluminum-containing adjuvants and by providing steric repulsion.

L12 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1991:478692 CAPLUS

DOCUMENT NUMBER: 115:78692

ORIGINAL REFERENCE NO.: 115:13435a,13438a

TITLE: The importance of surface charge in the optimization of antigen-adjuvant interactions

AUTHOR(S): Callahan, Patricia M.; Shorter, Andrew L.; Hem, Stanley L.

CORPORATE SOURCE: Dep. Pharm. Res., SmithKline Beecham Pharm., King of Prussia, PA, 19406-0939, USA

SOURCE: Pharmaceutical Research (1991), 8(7), 851-8
CODEN: PHREEB; ISSN: 0724-8741

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The absorptive behavior of the recombinant malarial antigens R32et32, R32NS181, and NS181V20 to aluminum hydroxide and aluminum phosphate gels was studied as a function of pH and buffer ions. The Plasmodium falciparum antigen, R32NS181, and the P. vivax antigen, NS181V20, with isoelec. points (pI) of 5.9 and 5.5, resp., adsorbed readily to the pos. charged boehmite form of aluminum hydroxide gel. These two antigens displayed reversible, linear adsorption behavior in the pH range 5-9, with maximal adsorption observed at the lowest pH studied. The addition of acetate buffer ions had little effect on adsorption, while the presence of phosphate decreased adsorption for R32NS181 and NS181V20 by 24 and 40%, resp. The adsorptive behavior of these two antigens with the neg. charged adjuvant, aluminum phosphate, was markedly decreased. The converse situation was observed with the R32et32 antigen, whose pI is estimated to be 12.8. There was minimal interaction of this antigen with aluminum hydroxide gel except in the presence of phosphate counter ions and significant, nonreversible adsorption with aluminum phosphate gel. Enhanced adsorption of R32et32 to aluminum hydroxide gel in the presence of phosphate is suggested to be the result of a covalent bond between a surface aluminum and a phosphate anion that modifies the surface charge of the aluminum hydroxide gel. These results indicate that the role of complementary surface charges, both for the ionization state of the protein and for the aluminum adjuvants, is the key in optimizing conditions for significant antigen-adjuvant interactions.

L12 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:583417 CAPLUS
DOCUMENT NUMBER: 107:183417
ORIGINAL REFERENCE NO.: 107:29325a,29328a
TITLE: The effect of surface-coupled antigen of liposomes in immunopotentiation
AUTHOR(S): Latif, Nahid Ali; Bachhawat, Bimal Kumar
CORPORATE SOURCE: Indian Inst. Chem. Biol., Calcutta, 700 032, India
SOURCE: Immunology Letters (1987), 15(1), 45-51
CODEN: IMLED6; ISSN: 0165-2478
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of surface coupled antigens of liposomes on the immunol. response was investigated. Lysozyme was covalently coupled to neutral and pos. charged liposomes using glutaraldehyde. S.c. administration of these preps. stimulated a significant antibody response higher than that elicited by the antigen entrapped in neutral liposomes. Immunization by liposomal antigens together with complete Freund's adjuvant resulted in strong immune responses, highest with the antigen coupled to neutral and pos. charged liposomes followed by the antigen entrapped in neutral liposomes. Primary and secondary immunization with lysozyme, both entrapped and coupled to liposomes, evoked an IgG response.

L12 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:520932 CAPLUS
DOCUMENT NUMBER: 107:120932
ORIGINAL REFERENCE NO.: 107:19495a,19498a
TITLE: Liposomes as immunological adjuvants: antigen incorporation studies
AUTHOR(S): Gregoriadis, Gregory; Davis, David; Davies, Alun
CORPORATE SOURCE: Sch. Med., R. Free Hosp., London, NW3 2QG, UK
SOURCE: Vaccine (1987), 5(2), 145-51
CODEN: VACCDE; ISSN: 0264-410X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tetanus toxoid was incorporated into liposomes composed of equimolar phospholipid and cholesterol. The toxoid was either passively entrapped into multilamellar vesicles prepared by the dehydration-rehydration procedure (DRV) or covalently coupled by diazotization to the surface of multilamellar vesicles (MLV) prepared by the classical procedure. Up to 82.3% of the antigen used was entrapped in neutral, neg. and pos. charged DRV composed of a variety of unsatd. and saturated phospholipids and 63.1% was coupled to MLV composed of egg phosphatidylcholine. After freeze-drying of toxoid-incorporating DRV and MLV and subsequent rehydration, up to 93.5% of the antigen was recovered with liposomes and, in the case of MLV, retained its external localization. Upon freeze-drying in the presence of 0.25M trehalose, up to 96.1% of the antigen was recovered with the DRV liposomes. In immunization studies using Balb/c mice, DRV composed of equimolar egg phosphatidylcholine and cholesterol acted as immunol. adjuvants to the entrapped tetanus toxoid. In addition, there was no difference in immune responses between DRV and MLV of identical composition but bearing the toxoid on their surface. A comparison of immune responses to the toxoid entrapped in DRV made of phospholipids with varying gel to liquid crystalline transition temperature (Tc) revealed a reduction in responses to very low values for DRV made of distearoylphosphatidylcholine (Tc 54°).

L12 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:3570 CAPLUS

DOCUMENT NUMBER: 106:3570
ORIGINAL REFERENCE NO.: 106:695a, 698a
TITLE: Effect of liposome charge on the intestinal absorption
of macromolecules and on the induced immune response
AUTHOR(S): Feknous, M.; Andre, F.; Andre, C.
CORPORATE SOURCE: UER Biol. Hum., Univ. Claude Bernard, Lyon, Fr.
SOURCE: Medecine et Hygiene (1986), 44(1667), 2158, 2160-1,
2164-5
CODEN: MEHGAB; ISSN: 0025-6749
DOCUMENT TYPE: Journal
LANGUAGE: French

AB As a model of oral vaccination, human serum albumin was given to mice in the free form or encapsulated in multilamellar phosphatidylcholine-cholesterol liposomes that were elec. neutral or charged neg. or pos. Compared with the intestinal absorption of the free albumin, that of the liposome-bound forms was increased 12-fold when the carrier was neutral and 3-fold when it was pos. or neg. charged. The immune response (as measured by the serum titer of antialbumin antibodies) was weak when the antigen was given in the free form or associated with the pos. charged liposome; it was greatly increased when the albumin was associated with the neutral or, especially, the neg. charged liposome.

This enhancement of the immune response was probably due both to increased intestinal absorption and to the adjuvant effect of the neg. charged carrier.

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